

Cerebrospinal fluid immunoglobulins in neurosyphilis*

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SUMMARY Using the fluorescent treponemal antibody-absorption (FTA-ABS) test and the solid phase haemadsorption assay (SPHA) *Treponema pallidum*-specific IgA was found in the cerebrospinal fluid (CSF) of patients with neurosyphilis but not in those with late latent syphilis. The presence of *T pallidum*-specific IgA in the CSF may inhibit the antitreponemal activity of IgG and thus play some part in the pathogenesis of neurosyphilis.

Introduction

The occurrence of *Treponema pallidum*-specific immunoglobulins has been studied extensively during recent years and serological methods for the diagnosis of syphilis have become both specific and easy to perform. Since the development of the solid phase haemadsorption assay (SPHA) for the routine demonstration of *T pallidum*-specific 19S-IgM, even syphilitic reinfection can be easily diagnosed serologically and treatment failures can be detected.

Little is known about the presence and quantitative distribution of *T pallidum*-specific immunoglobulins in the cerebrospinal fluid (CSF) of patients with neurosyphilis. The present study was performed to investigate these specific immunoglobulins (Ig) A and G in the CSF of patients with neurosyphilis and of those with late latent syphilis without involvement of the central nervous system (CNS).

Patients and methods

NEUROSYPHILIS

Six patients (four men and two women), aged 53-79 years, had signs or symptoms of neurosyphilis or both (table I). All had high titres in the *T pallidum* haemagglutination assay (TPHA-CSF) ranging from

2560-40 960. The TPHA indices* were above 100, thus strongly suggesting neurosyphilis (unpublished data).

LATE LATENT SYPHILIS

Six patients (three men and three women) aged 49-79 years with late latent syphilis but no CNS involvement were investigated (table II). The CSF-TPHA titres were low (ranging from 40-640) and the TPHA indices were all below 100.

SEROLOGICAL TECHNIQUES

The presence of *T pallidum*-specific IgG and IgA was determined both by the FTA-ABS test (using FITC-conjugated heavy-chain monospecific antisera, DAKO, diluted 1/30 for IgA and 1/200 for IgG) and by the SPHA with the same reagents.¹

Results

T PALLIDUM-SPECIFIC IMMUNOGLOBULINS

IgG

T pallidum-specific IgG was present in the serum and the CSF of all the patients studied. There were no significant differences in the quantitative distribution between the group of patients with neurosyphilis and those without CNS involvement (table III).

IgA

T pallidum-specific IgA was detected by the SPHA in the serum of all the patients with neurosyphilis (mean

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*TPHA index = $\frac{\text{CSF-TPHA titre}}{\text{albumin quotient}}$

$\left(\text{albumin quotient} = \frac{\text{CSF albumin (mg/dl)} \times 10^3}{\text{Serum albumin (mg/dl)}} \right)$

TABLE I Results of serological tests in serum and cerebrospinal fluid of patients with neurosyphilis

Patient No	Clinical diagnosis	Serum				Cerebrospinal fluid					
		VDRL titre	TPHA titre	FTA-ABS	Albumin (mg/100ml)	VDRL titre	TPHA titre	FTA-ABS	Cells ($\times 10^6/l$)	Albumin (mg/100ml)	TPHA index
1	Meningovascular syphilis	1/2	1/10 240	++	3900	1/2	1/10 240	++	2	26	1530
2	Taboparesis	1/2	1/20 480	+++	3700	1/2	1/10 240	++	2	28	1700
3	General paresis	1/4	1/20 480	++	4200	1/1	1/2 560	++	52	68	160
4	General paresis	1/16	1/20 480	+++	5900	1/2	1/10 240	+++	3	140	435
5	Taboparesis	1/1	1/5120	+++	3560	1/1	1/2 560	+++	3	63	144
6	Taboparesis	1/16	1/81 920	+++	2480	1/1	1/40 960	+++	2	12	8200

++ and +++ = positive

TABLE II Results of serological tests in serum and cerebrospinal fluid of patients with late latent disease but without symptoms of neurosyphilis

Patient No	Serum				Cerebrospinal fluid					
	VDRL titre	TPHA titre	FTA-ABS	Albumin (mg/100ml)	VDRL titre	TPHA titre	FTA-ABS	Cells ($\times 10^6/l$)	Albumin (mg/100ml)	TPHA index
7	1/32	1/20 480	++	5000	—	1/160	++	0.3	17	45
8	1/1	1/160	++	2700	—	1/40	++	0.0	18	23
9	—	1/320	++	4200	—	1/40	++	0.3	22	8
10	1/2	1/640	++	2280	—	1/10	++	—	11	2
11	—	1/10 240	++	1840	—	1/40	++	0.0	9	8
12	1/1	1/20 480	+++	3870	—	1/640	+++	6	40.5	64

++ and +++ = positive; — = negative

TABLE III *T pallidum*-specific IgG and IgA in the serum and CSF of patients with late syphilis with (Nos 1-6) and without (Nos 7-12) involvement of the central nervous system

Patient No	IgG-FTA test		IgA-SPHA test		IgA-FTA test	
	Serum	CSF	Serum	CSF	Serum	CSF
1	+++	+++	1/16	1/2	—	+
2	++++	+++	1/8	1/2	ND	ND
3	+++	+++	1/4	1/2	—	++
4	+++	+++	1/1	1/1	—	+++
5	++++	+++	1/1	1/1	—	—
6	++++	+++	1/2	1/4	—	++
7	++	++	—	—	—	—
8	+	+	—	—	—	—
9	++	+++	—	—	—	—
10	++	++	—	—	—	—
11	++	++	—	—	—	—
12	+++	+++	—	—	—	—

ND = not done; +, ++, +++ and ++++ = positive; — = negative

titre, 5.3) but in none of the patients without neurosyphilis (table III). IgA was consistently present in the CSF of the patients with neurosyphilis (mean titre, 2.0) but could not be detected in the CSF of those without neural involvement (table III).

Discussion

This study demonstrates differences in the distribution of CSF immunoglobulins in patients with neuro-

syphilis and in those without evidence of neurosyphilis. *T pallidum*-specific IgA in the CSF may indicate syphilitic involvement of the CNS.

The origin of CSF-IgA in patients with neurosyphilis has not yet been clarified. Since in this study IgA was detected in the CSF as well as in the serum at comparatively high titres, it may be transferred passively from the serum to the CSF or be produced in the CNS in close proximity to the CSF or both.

At first glance the presence of immunoglobulins in an infectious disease leads one to assume that

increased immune defence mechanisms are operative against the causative micro-organism. In this respect it is of interest that IgA has recently been shown to enhance the virulence of *Neisseria meningitidis*² and *Candida albicans*, possibly by inhibiting IgG bactericidal activity.³ IgA seems to compete with IgG molecules at the Ig receptor sites on the target micro-organism. Since, however, IgA does not cause cytotoxicity by activating the classical complement pathway, the simultaneous presence of IgA and IgG, in fact, decreases the antibacterial effects of IgG.

Preliminary evidence thus indicates that the presence of *T pallidum*-specific IgA in the CSF of patients with neurosyphilis may be responsible for

inhibiting the antitreponemal activity of CSF-IgG and thus play a role in the pathogenesis of neurosyphilis. Studies are in progress to investigate the role of IgA in the natural course of other stages of the disease.

References

1. Schmidt, BL. Solid phase hemadsorption. A method for rapid detection of *Treponema pallidum*-specific IgM. *Sex Transm Dis* 1980; 7: 51-8.
2. McLeod-Griffis J. Bactericidal activity of meningococcal antisera. *J Immunol* 1975; 11: 1779-84.
3. Wilton JMA. Suppression by IgA of IgG-mediated phagocytosis. *Clin Exp Immunol* 1978; 34: 423-8.